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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,495	01/20/2006	Elliott A Gruskin	127304.00901	6177

21269 7590 03/30/2010

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EXAMINER	
PROUTY, REBECCA E	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
03/30/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,495	GRUSKIN ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/21/10 has been entered.

Claims 1-26 have been canceled and newly presented claims 27-35 are still at issue and are present for examination.

Applicants' arguments filed on 1/21/10, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27-31 and 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olsen et al. (WO 00/64482) in view of either of Yick et al. (reference C1 of applicants IDS of 7/07) or Zuo et al. (reference CAG of applicants IDS of 4/06)

Olsen et al. teach a chimeric protein composed of two portions a first component capable of suppressing or neutralizing a neurite growth inhibitory molecule and a second component capable of stimulating neurite growth and/or regeneration. (see page 4) and pharmaceutical compositions thereof. Olsen et al. specifically teach that the component capable of stimulating neurite growth and/or regeneration can be a neurotrophic molecule including NGF, BDNF, NT3, FGF and many others (see page 10). Olsen et al. further teach that the neurite growth inhibitory molecule which is inhibited or suppressed by the first component of the chimeric molecule includes chondroitin proteoglycans (see page 25). Olsen et al. further teach that the two components of the chimeric molecule may be optionally separated by a peptide linker (see page 8). Olsen et al. do not explicitly teach that the component capable of suppressing or neutralizing a neurite growth inhibitory

molecule is a polypeptide possessing matrix modification activity or particularly a chondroitinase such as chondroitinase ABC.

Each of Yick et al. and Zuo et al. teach that chondroitin proteoglycans are extracellular matrix components which inhibit neuronal growth and regeneration following injury and that the administration of chondroitinase ABC which degrades chondroitin proteoglycans promotes axonal regeneration.

Therefore, it would have been obvious to one of ordinary skill in the art to select chondroitinase ABC as the component capable of suppressing or neutralizing a neurite growth inhibitory molecule in the chimeric molecule of Olsen et al. as the disclosures of Yick et al. and Zuo et al. show that chondroitinase ABC has all the properties that are preferred in this component as disclosed by Olsen et al. Furthermore, claims 34 and 35 are included in the rejection as pharmaceutical compositions of the chimeric proteins would have been obvious to one of ordinary skill in the art and determining the optimum therapeutic dose of a desired pharmaceutical composition is well within the ordinary skill in the art.

Applicants argue that Olsen discloses an "amphibody" comprised of at least two components, wherein the first component, the "anti-end," is antibody-based and capable of

locating and binding to inhibitory molecules in a tissue environment. However, applicants characterization of Olsen is narrow and not inclusive of all that Olsen teaches. The "anti-end" of the chimeric protein of Olsen is not restricted to antibodies and is not taught to solely have the function of localization and binding. This end of the chimeric protein disclosed by Olsen et al. is specifically disclosed as including inhibitors/suppressors of proteoglycans (see page 22) and in particular chondroitin proteoglycans (page 25) and is explicitly disclosed as having the function of "suppressing or neutralizing a neurite growth inhibitory effect" (see page 4). Applicants argue that in the claimed chimeric protein the first peptide sequence is an enzyme which in contrast to the "anti-end" of the chimera of Olsen does not specifically bind and sequester an inhibitory antigen converting an inhibitory site into a stimulatory one. However, this is in fact incorrect as enzymes do in fact bind their substrates and thus the enzyme of the claimed chimeric protein will in fact also function to localize the "pro-end" having neural growth stimulatory activity and thus will in fact act to convert an inhibitory site to a stimulatory site. While the claimed enzymes as noted by applicants will in fact degrade the proteoglycans and thus eventually will destroy the inhibitory site, this will not in fact destroy the intended

function of the chimeric protein of Olsen et al. as argued by applicants as the degradation of the substrate will only occur after the substrate is bound by the chimeric protein and the function of localizing the "pro-end" to the correct site has been accomplished.

Applicants argue that substituting the prior art amphibody's first component with chondroitinases, hyaluronidases, or matrix metalloproteinases would destroy the amphibody's ability to inhibit the function of proteoglycans by hindering them while keeping their structure intact and further results in the destruction of the target proteoglycans, and not merely inhibition of the proteoglycans through use of an antibody. However, this is not persuasive because it suggests an advantage of the prior art amphibody not in fact disclosed in Olsen. Nowhere in the disclosure of Olsen et al. is it taught or even suggested that keeping the structure of the inhibitory molecule intact is important and thus the fact that the enzymes of the instant claims will not act in this fashion in no way destroys the functions of the prior art amphibody. The functions of the prior art molecule disclosed by Olsen et al. are localization and suppression of the inhibitory activity. BOTH of these functions would be maintained in the chimeric protein suggested in the instant rejection. As previously discussed

enzymes do bind to their substrates and thus will accomplish the localization function and clearly degradation of chondroitin proteoglycans will suppress all inhibitory activities thereof. Furthermore, the teachings of Yick et al. and Zuo et al. make it clear that in fact degradation of chondroitin proteoglycans in particular does not have harmful effects as administration of this enzyme in fact promotes axonal regeneration.

Applicants further argue that one skilled in the art would have no reasonable expectation of success that a chimeric protein comprising an enzyme and a second polypeptide possessing regenerating activity for neural cells as claimed would exhibit the requisite activity because Olson merely teaches that the proteoglycan activity is to be inhibited through use of an antibody, which does not change the milieu and thus there is no teaching or suggestion that using an enzymatic moiety that destroys the proteoglycan and significantly changes the milieu, would otherwise result in axonal growth when combined with the second component of Olson's amphibody. However, this is not persuasive because it ignores the teaching of Yick et al. and Zou et al. that degradation of chondroitin proteoglycans does not have harmful effects as administration of this enzyme in fact promotes axonal regeneration. This teaching makes clear

that degradation of the milieu will not prevent axonal regeneration.

Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Olsen et al. (WO 00/64482) in view of either of Yick et al. or Zuo et al. as applied to claims 27-31 and 33-35 above, and further in view of Gearing (US Patent 5,262,522).

Olsen et al., Yick et al. and Zuo et al. are discussed above but do not explicitly disclose the use of an immunoglobulin Fc portion as the peptide linker between the two portions of the chimeric protein.

Gearing et al. teach a chimeric protein having two separate polypeptide domains optionally separated by a peptide linker. Gearing et al. teach that a preferred peptide linker is an immunoglobulin Fc portion (see column 8, lines 17-43).

Therefore, it would have been obvious to one of ordinary skill in the art to select an immunoglobulin Fc portion as the peptide linker of the chimeric molecule of Olson et al. as Gearing et al. specifically teach this as a preferred linker molecule for another chimeric protein formed by the conjugation of two proteins which don't naturally occur together.

Applicant has not presented any arguments specifically traversing this rejection but instead relies upon the traversal

discussed above. Therefore, this rejection is maintained for the reasons presented above.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached at (571) 272-0811. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652